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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/932,300	08/17/2001	Eric Garver	9855-3U2	5387

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EXAMINER	
LACOURCIERE, KAREN A	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 03/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/932,300	GARVER ET AL.	
	Examiner	Art Unit	
	Karen A. Lacourciere	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-59* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse on December 11, 2003 is noted and appreciated, however, the restriction requirement set forth in the Office Action mailed June 11, 2003 by the prior Examiner does not appear correct and therefore, a new restriction requirement is set forth in this Office action, as follows.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-24, 33-40 and 50, drawn to an antisense oligonucleotide for inhibiting the expression of an aldehyde dehydrogenase gene in a cell, classified in class 536, subclass 24.5.

II. Claims 25-32, 41-43, and 51-54 drawn to a method of decreasing ethanol tolerance in a human including wherein the desire to consume alcohol is decreased, classified in class 514, subclass 44.

III. Claim 44, drawn to a method of making an antisense oligonucleotide, classified in class 536, subclass 25.3.

IV. Claims 45-50, drawn to an antisense oligonucleotide for inhibiting the expression of a gene that encodes TNF-alpha, classified in class 536, subclass 24.5.

V. Claim 58, drawn to a method of predicting the efficacy of an oligonucleotide for inhibiting the expression of a gene, classified in class 435, subclass 6.

VI. Claim 59, drawn to a method of separating from a mixture of oligonucleotides an antisense oligonucleotide efficacious for inhibiting the expression of a gene, classified in class 435, subclass 6.

Claim 50 link(s) inventions I and IV. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claim 50. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01. The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the antisense oligonucleotide of group I can be used in a materially different method of using the

antisense than the method of treatment of Group II. For example, the antisense oligonucleotide of Group I can be used in a cell in vitro to inhibit the expression of aldehyde dehydrogenase for enzymatic pathway studies, or as a probe or primer, all of which are materially different than the methods of Group II.

Inventions I and III are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the antisense of Group I can be made in a materially different method than that of Group III. For example, the antisense of Group I can be made by screening for antisense to aldehyde dehydrogenase using a micro array of all sequences, without any focus on the motif specified by the synthesis method of Group III.

Inventions I and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to materially different antisense (e.g., structurally unrelated sequences) with different functions. For example, the antisense of Group I functions to inhibit the expression of aldehyde dehydrogenase, which is different than the antisense of Group IV, which functions to inhibit the expression of TNF-alpha.

Inventions I and V are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the antisense of Group I can be used in a materially different method than the method of Group V, for example, the antisense of Group I can be used in a method of treatment for alcoholism, which is materially different than the method of predicting efficacy of Group V

Inventions I and VI are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the antisense of Group I can be made by a materially different method than the method of synthesis of Group VI. For example, the antisense of Group I can be made by screening for antisense to aldehyde dehydrogenase using a microarray, which is materially different than the separation method of Group VI.

Inventions II and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to materially different methods with different effects. For example, the methods of treatment of Group II has the effect of

decreasing alcohol tolerance, whereas the method of Group III has the effect of determining the sequence of antisense to a target gene.

Inventions II and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to a method and a product that is not used in the method, wherein the method and the product have different functions. For example, the method of Group II has the effect of decreasing tolerance of alcohol in a subject by the inhibition of the expression of aldehyde dehydrogenase, whereas the antisense of Group IV functions to inhibit the expression of TNF-alpha.

Inventions II and V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to materially different methods with different effects. For example, the method of Group II has the effect of decreasing tolerance of alcohol in a subject by the inhibition of the expression of aldehyde dehydrogenase, whereas the method of Group V functions to determine the efficacy of an antisense oligonucleotide.

Inventions II and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to materially different methods with

different effects. For example, the method of Group II has the effect of decreasing tolerance of alcohol in a subject by the inhibition of the expression of aldehyde dehydrogenase, whereas the method of Group VI functions to separate an antisense oligonucleotide from a mixture of oligonucleotides.

Inventions III and IV are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the antisense of Group IV can be made in a materially different method than that of Group III. For example, the antisense of Group IV can be made by screening for antisense to TNF-alpha using a micro array of all sequences, without any focus on the motif specified by the synthesis method of Group III.

Inventions III and V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to materially different methods with different effects. For example, the methods of Group III have the effect of making an oligonucleotide, whereas the methods of Group V have the effect of predicting the efficacy of an oligonucleotide.

Inventions III and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of

operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to materially different methods with different effects. For example, the methods of Group III have the effect of making an oligonucleotide by synthesis, whereas the methods of Group VI have the effect of separating an oligonucleotide from a mixture of oligonucleotides.

Inventions IV and V are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the antisense of Group IV can be used in a materially different method than the method of Group V, for example, the antisense of Group IV can be used in a method of inhibiting the expression of TNF-alpha in a cell, which is materially different than the method of predicting efficacy of Group V.

Inventions IV and VI are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the antisense of Group IV can be made by a materially different method than the method of synthesis of Group VI. For example, the antisense of Group I can be made by screening for antisense to TNF-alpha using a microarray, which is materially different than the separation method of Group VI.

Inventions V and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to materially different methods with different effects. For example, the methods of Group V have the effect of predicting the efficacy of an antisense oligonucleotide, whereas the methods of Group VI have the effect of separating an oligonucleotide from a mixture of oligonucleotides.

Single Sequence Election Applicable to Groups I and IV

Pursuant to 35 U.S.C. 121 and 37 C.F.R. 1.141, the antisense sequences listed in claims 5, 13, 14, 15, 36, and 49 are subject to restriction. The Commissioner has partially waived the requirements of 37 C.F.R. 1.141 and will permit a reasonable number of such nucleotide sequences to be claimed in a single application. Under this policy, up to 10 of independent and distinct nucleotide sequences will be examined in a single application. (see MPEP 803.04 and 2434)

Claims 5, 13, 14, 15 and 36 specifically claims antisense SEQ ID NOS 98, 107, 108, 109, 110 and 111 and, which are targeted to and inhibit the expression of aldehyde dehydrogenase in a cell and Claim 49 specifically claims antisense target to regions I-XXII of TNF-alpha. Although the antisense sequences claimed each target and inhibit the expression of the a particular gene, the instant antisense sequences are considered to be unrelated, since each antisense sequence claimed is structurally and functionally

independent (with respect, for example to sequence structure) and distinct for the following reasons: each antisense sequence has a unique nucleotide sequence, each antisense sequence targets a different and specific region of aldehyde dehydrogenase or TNF-alpha, and each antisense, upon binding to aldehyde dehydrogenase or TNF-alpha, functionally decreases the expression of the aldehyde dehydrogenase or TNF-alpha and to a varying degree. Furthermore, a search of more than one (1) of the antisense sequences claimed in claims 5, 13, 14, 15, 36 and 49 presents an undue burden on the Patent and Trademark Office due to the complex nature of the search and corresponding examination of more than one (1) of the claimed antisense sequences. In view of the foregoing, one (1) antisense sequence is considered to be a reasonable number of sequences for examination. Accordingly, applicants are required to elect one (1) antisense sequence from claim 5, 13, 14, 15, 36 and 49.

Specifically, if Applicant should elect Group I for examination, Applicant must elect either ALDH2-1 allele or ALDH2-2 allele and one sequence selected from SEQ ID NO: 98, 107, 108, 109, 110 and 111, wherein the sequence correspond to the elected allele.

If Applicant should elect Group IV for examination, Applicant must elect an antisense oligonucleotide complementary to one of regions I-XXII of TNF-alpha.

Applicant should note, if any of Groups II, III, V or VI are elected for examination and during the prosecution of the case specific SEQ ID NO's are introduced into the claims, at that point Applicant will be required to elect a single sequence for examination.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Lacourciere whose telephone number is (571) 272-0759. The examiner can normally be reached on Monday-Thursday 7:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (571) 272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Lacourciere
March 8, 2004

KAREN A. LACOURCIERE, PH.D
PRIMARY EXAMINER